

RESPIRATORY SYNCYTIAL VIRUS VACCINES EXPRESSING PROTECTIVE ANTIGENS FROM PROMOTOR-PROXIMAL GENES

ABSTRACT OF THE DISCLOSURE

5 Recombinant respiratory syncytial virus (RSV) having the position of genes
shifted within the genome or antigenome of the recombinant virus are infectious and
attenuated in humans and other mammals. Gene shifted RSV are constructed by insertion,
10 deletion or rearrangement of genes or genome segments within the recombinant genome or
antigenome and are useful in vaccine formulations for eliciting an anti-RSV immune
response. Also provided are isolated polynucleotide molecules and vectors incorporating a
recombinant RSV genome or antigenome wherein a gene or gene segment is shifted to a
15 more promoter-proximal or promoter-distal position within the genome or antigenome
compared to a wild type position of the gene in the RSV gene map. Shifting the position of
genes in this manner provides for a selected increase or decrease in expression of the gene,
depending on the nature and degree of the positional shift. In one embodiment, RSV
glycoproteins are upregulated by shifting one or more glycoprotein-encoding genes to a more
20 promoter-proximal position. Genes of interest for manipulation to create gene position-
shifted RSV include any of the NS1, NS2, N, P, M, SH, M2(ORF1), M2(ORF2), L, F or G
genes or a genome segment that may be part of a gene or extragenic. A variety of additional
mutations and nucleotide modifications are provided within the gene position-shifted RSV of
the invention to yield desired phenotypic and structural effects.

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